AMENDMENTS TO THE SPECIFICATION

Please replace paragraph 1 at page 1 with the following amended paragraph.

[0001] This application is a continuation-in-part of: (1) ~~pending~~ abandoned U.S. application Ser. No. 09/675,470, filed September 28, 2000, which ~~is a continuation-in-part of~~ claims priority from abandoned U.S. provisional application Ser. No. 60/161,453, filed October 25, 1999, and (2) ~~pending~~ abandoned U.S. provisional application Ser. No. 60/272,624, filed March 1, 2001, and (3) ~~pending~~ abandoned U.S. provisional application Ser. No. 60/323,016, filed September 10, 2001, and (4) ~~pending~~ abandoned U.S. provisional application Ser. No. 60/340,045, filed November 1, 2001, and (5) ~~pending~~ abandoned U.S. provisional application Ser. No. 60/328,738, filed October 11, 2001, and (6) ~~pending~~ abandoned U.S. provisional application Ser. No. 60/338,015, filed November 8, 2001, and (7) ~~pending~~ abandoned U.S. provisional application Ser. No. 60/343,523, filed December 20, 2001, and (8) ~~pending~~ abandoned U.S. application Ser. No. 09/820,483, filed March 29, 2001, which is a continuation-in-part of ~~pending~~ abandoned U.S. application Ser. No. 09/535,675, filed March 23, 2000, now patent No. 6,667,299, which ~~is a continuation-in-part of~~ claims priority from abandoned U.S. provisional application Ser. No. 60/126,056, filed March 23, 1999, and abandoned U.S. provisional application Ser. No. 60/124,087, filed March 11, 1999 and which is a continuation-in-part of abandoned U.S. application Ser. No. 09/449,004, filed November 24, 1999, which ~~is a continuation-in-part of~~ claims priority from abandoned U.S. provisional application Ser. No. 60/109,923, filed November 24, 1998, and which is a continuation-in-part of abandoned U.S. application Ser. No. 09/449,184, filed November 24, 1999, which ~~is a continuation-in-part of~~ claims priority from abandoned U.S. provisional application Ser. No. 60/109,924, filed November 24, 1998, and which is a continuation-in-part of abandoned U.S. application Ser. No. 09/449,042, filed November 24, 1999, which ~~is a continuation-in-part of~~ claims priority from

abandoned U.S. provisional application Ser. No. 60/110,127, filed November 27, 1998, and which is a continuation-in-part of ~~pending~~ abandoned U.S. application Ser. No. 09/461,026, filed December 15, 1999, which ~~is a continuation-in-part of~~ claims priority from abandoned U.S. provisional application Ser. No. 60/112,206, filed December 15, 1998, and which is a continuation-in-part of abandoned U.S. application Ser. No. 09/586,673, filed June 1, 2000, which ~~is a continuation-in-part of~~ claims priority from abandoned U.S. provisional application Ser. No. 60/145,823, filed July 27, 1999, and which is a continuation-in-part of abandoned U.S. application Ser. No. 09/586,672, filed June 1, 2000, which ~~is a continuation-in-part of~~ claims priority from abandoned U.S. provisional application Ser. No. 60/137,745, filed June 3, 1999, and which is a continuation-in-part of abandoned U.S. application Ser. No. 09/414,905, filed October 8, 1999, which ~~is a continuation-in-part of~~ claims priority from abandoned U.S. provisional application Ser. No. 60/140,028, filed June 16, 1999, all of which are incorporated herein by reference in their entireties.

Please replace paragraph 56 at page 12 with the following amended paragraph.

[0056] Other embodiments include a method to enhance the expression of one or more cytokines or interleukins that ~~facilitate Th1 or Tc1 immune responses~~ facilitate Th1 or Tc1 immune responses in a subject or to reduce the expression of one or more cytokines or interleukins that facilitate Th2 or Tc2 immune response in a subject comprising administering to the subject an ~~effective amount of of~~ effective amount of a formula 1 compound, whereby the subject's Th1 or Tc1 immune ~~response is enhanced or the~~ response is enhanced or the subject's undesired Th2 or Tc2 immune response is reduced.

Please replace paragraph 66 at page 13 with the following amended paragraph.

[0056] As used here, "excipients" include liquids, such as benzyl benzoate, cottonseed oil, N,N-dimethylacetamide, a C_{2-12} alcohol (e.g., ethanol), glycerol, peanut oil, a polyethylene glycol ("PEG"), vitamin E, poppyseed oil, propylene glycol, safflower oil, sesame oil, soybean oil and vegetable oil. Any solid excipient may be a fine powder or granulated. Excipients, as used herein may optionally exclude one or more excipient, e.g., chloroform, dioxane, vegetable oil, DMSO, other excipients or any combination of these. Excipients include one or more components typically used in the pharmaceutical formulation arts, e.g., one, two or more of fillers, binders, disintegrants, dispersants, preservatives, glidants and lubricants. Exemplary excipients include povidone, crospovidone, corn starch, carboxymethyl cellulose, hydroxypropyl methylcellulose, microcrystalline cellulose, gum arabic, polysorbate 80, butylparaben, propylparaben, methylparaben, BHA, EDTA, sodium lauryl sulfate, sodium chloride, potassium chloride, titanium dioxide, magnesium stearate, castor oil, olive oil, vegetable oil, buffering agents such as sodium hydroxide, monobasic sodium phosphate, dibasic sodium phosphate, potassium hydroxide, monobasic potassium phosphate, dibasic potassium phosphate, tribasic potassium phosphate, potassium carbonate, potassium bicarbonate, ammonium hydroxide, ~~ammouium chloride, saccharides such as~~ ammonium chloride, saccharides such as mannitol, glucose, fructose, sucrose or lactose any of which may be compressible or any of which may be spray dried.

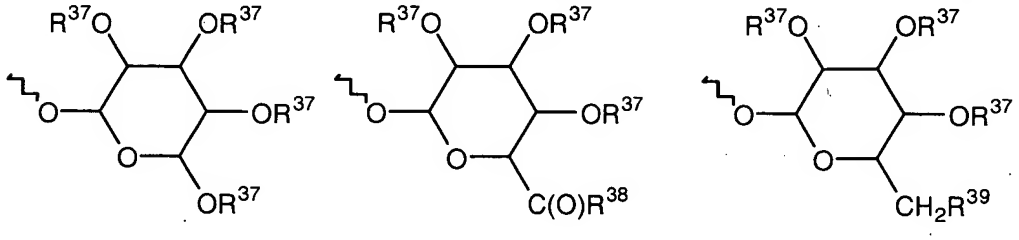
Please replace paragraph 68 at page 14 with the following amended paragraph.

[0068] The terms "effective amount", "effective dose" or the like mean an amount of a formula 1 compound that is sufficient to elicit a desired response, e.g., restoration of normal immune responsiveness in an immunodeficient subject to which it is administered or to detectable modulation or amelioration of an

immune or cellular parameter or a clinical condition or symptom. ~~An effective amount may be a a single~~ An effective amount may be a single dose or two or more subdoses of a formula 1 compound administered in one day, or it may be administered as multiple doses over a period of time, e.g., over 2 days to about 1 year.

Please replace paragraph 109 at page 26 with the following amended paragraph.

[00109] As used herein, "monosaccharide" means a polyhydroxy aldehyde or ketone having the empirical formula $(CH_2O)_n$ where n is 3, 4, 5, 6 or 7. Monosaccharide includes open chain and closed chain forms, but will usually be closed chain forms. Monosaccharide includes hexofuranose and pentofuranose sugars such as 2'-deoxyribose, ribose, arabinose, xylose, their 2'-deoxy and 3'-deoxy derivatives and their 2',3'-dideoxy derivatives. Monosaccharide also includes the 2',3' dideoxydidehydro derivative of ribose. Monosaccharides include the D-, L- and DL-isomers of glucose, fructose, mannose, idose, galactose, allose, gulose, altrose, talose, fucose, erythrose, threose, lyxose, erythrulose, ribulose, xylulose, ribose, arabinose, xylose, psicose, sorbose, tagatose, glyceraldehyde, dihydroxyacetone and their monodeoxy or other derivatives such as rhamnose and glucuronic acid or a salt of glucuronic acid. Monosaccharides are optionally protected or partially protected. ~~Exemplary monosacharides include~~ Exemplary monosaccharides include



Please replace paragraph 111 at page 26 with the following amended paragraph.

[00111] Optionally substituted alkyl group, optionally substituted alkenyl group, optionally substituted alkynyl group, optionally substituted aryl moiety and optionally substituted heterocycle mean an alkyl, alkenyl, alkynyl, aryl or heterocycle moiety that contains an optional substitution(s). ~~Such moieties include include~~ Such moieties include C_{1-20} alkyl moieties, C_{2-20} alkenyl moieties, C_{2-20} alkynyl moieties, aryl moieties, C_{2-9} heterocycles or substituted derivatives of any of these. Typical substitutions for these organic groups are as described above for substituted alkyl moieties and include, e.g., 1, 2, 3, 4, 5, 6 or more, independently selected -O-, -S-, -NR^{PR}-, -C(O)-, -$N(R^{PR})_2$, -C(O)OR^{PR}, -$OC(O)R^{PR}$, -OR^{PR}, -SR^{PR}, -NO_2, -CN, -NHC(O)-, -C(O)NH-, -OC(O)-, -C(O)O-, -O-A8, -S-A8, -C(O)-A8, -OC(O)-A8, -C(O)O-A8, =N-, -N=, -OPO_2R^{PR}, -OSO_3H or halogen moieties or atoms, where R^{PR} independently is -H, a protecting group or both R^{PR} together are a protecting group and A8 is C_{1-8} alkyl, C_{1-8} alkenyl, C_{1-8} alkynyl, C_{1-4} alkyl-aryl (e.g., benzyl), aryl (e.g. phenyl) or C_{1-4} alkyl-C_{1-5} heterocycle. Substitutions are independently chosen. The organic moieties as described here, and for other any other moieties described herein, exclude obviously unstable moieties, e.g., -O-O-, except where such unstable moieties are transient species that one can use to make a compound with sufficient chemical stability for the one or more of the uses described herein.

Please replace paragraph 126 at page 30 with the following amended paragraph.

[00126] "Steroid receptor" means a gene product, typically a protein monomer or dimer that can bind to a ligand, e.g., a natural steroid, a steroid analog, or another ligand such as a formula 1 compound or a metabolic precursor thereof or a metabolite thereof, a lipid, e.g., a prostaglandin, or the like. Steroid receptors include orphan steroid receptors. Orphan steroid receptors are proteins for which the natural ligand or biological function is at least partially unknown. As used

here, steroid receptors include homodimers, e.g., SXR and $(CAR\beta)_2$, and heterodimers, e.g., PXR-CARβ or RXR-CARβ. Steroid receptors also include isoforms, e.g., PXR.1 and PXR.2 for the PXR receptor, and homologs of the steroid receptors, e.g., the homolog of CARβ known as MB67. Isoforms are typically generated by different splicing pathways for a nuclear RNA from one gene, while homologs are typically a distinct copy of a steroid receptor gene, where the gene copy encodes only relatively small differences compared to the reference steroid receptor gene product. Such differences are most often found in areas other than the dimerization region and the steroid binding region of the steroid receptor's structure. Typically isoforms and homologs bind the same or similar ligands as the reference gene product or steroid receptor. Steroid receptors may be of human or animal origin, e.g., obtained from cells, tissues or cDNA expression libraries derived from cells or tissues of any primate, rodent (including murine), avian, ovine, bovine, equine, canine or feline species or any of the species or any species within any group (e.g., Family or Genus) of species mentioned elsewhere herein or in any reference cited herein. Modulation of steroid receptors by formula 1 compounds can arise from (1) their direct interaction with a steroid receptor or a cofactor thereof or (2) indirect effects such as (A) detectably increased or ~~decreased synthesis or level of the steroiud receptor~~ decreased synthesis or level of the steroid receptor or (B) generation of a signal or stimulus that leads to detectable modulation of one or more biological activities of the receptor, e.g., detectable inhibition of steroid receptor mediated gene transcription or detectable enhancement of steroid receptor mediated gene transcription.

Please replace paragraph 142 at page 37 with the following amended paragraph.

[00142] Tripeptides, i.e., 3 linked amino acid residues, are also useful embodiments. Each amino acid in a tripeptide may be in an L, D or mixed

configuration. Tripeptides include those where A, C, D, E, F, G, H, I, K, L, M, N, P, Q, R, S, T, V, W or Y is linked by a standard peptide bond to the amino or the carboxyl terminus of any of the dipeptides listed above. The sequence –X1-pro-X2- (where X1 is any amino acid and X2 is hydrogen, any amino acid residue or a carboxyl ester of proline) will be cleaved by luminal carboxypeptidase to yield X1 with a free carboxyl, which in turn autocatalytically cleaves the amidate bond. X2 usually will be a benzyl ester of the carboxy group of X2. Other embodiments include tetrapeptides such as ones where any two of the dipeptides listed above, which may be the same or different dipeptides (e.g., AA and AA linked together or, e.g., AA and GI linked together), are linked to each other by a peptide bond through the amino terminus or carboxyl terminus. One, 2 or more ~~tetrapeptides may bonded to the~~ tetrapeptides may be bonded to the formula 1 or formula 2 compound through the tetrapeptide's amino or carboxyl terminus.

Please replace paragraph 179 at page 48 with the following amended paragraph.

[00179] Other embodiments include a product produced by the process of contacting BrEA hemihydrate, which may be substantially free of other forms of BrEA, with an excipient suitable for human pharmaceutical use or for veterinary use. The product is useful to make formulations or unit dosage forms that contain the hemihydrate. ~~Exemplary excipients include or or~~ Exemplary excipients include or more of those disclosed herein, e.g., sucrose, mannitol, starch, carboxymethyl cellulose, magnesium stearate and the like.

Please replace paragraph 183 at page 49 with the following amended paragraph.

[00183] In other embodiments, one or more of R^1-R^6, R^{10}, R^{15}, R^{17} and R^{18}, usually one, comprises an amino acid or a peptide, while the remaining groups

are independently selected from the moieties defined herein. In these embodiments, the peptides are typically dimers (dipeptides) or trimers (tripeptides). For example one of R^1, R^2 or R^4 comprises an amino acid, the remaining of R^1, R^2 or R^4 independently comprise -OH, =O, an ester, a carbonate or a carbamate, while R^3 is a halogen, hydroxyl or an ester and R^5 and R^6 independently are -H, $-(CH_2)_n-CH_3$, $-(CH_2)_n-CH_2OH$, or $-(CH_2)_n-CH_2F$, $-(CH_2)_{2-4}-O-(CH_2)_{2-4}-CH_3$, where n is 0, 1, 2, 3, 4, 5, 6, 7 or 8 often 0, 1, or 2, usually 0. Typically the ester, ~~carbonate or carbamate are hydrolyzable~~ carbonate or carbamate is hydrolyzable under physiological conditions.

Please replace paragraph 314 at page 99 with the following amended paragraph.

[00314] The individual compounds and genera named in groups 1-54 above may also be named using any suitable formal or informal chemical nomenclature. Thus, as will be apparent, ~~individual compounds in these groups incude~~ individual compounds in these groups include 16α-bromoepiandrosterone, 16α-hydroxyepiandrosterone, 3α,16α-dihydroxy-5α-androstane-17-one, 3α,16α,17β-trihydroxy-5α-androstane, 3α,16α,17α-trihydroxy-5α-androstane, 3β,17β-dihydroxyandrost-5-ene or 3β,7β,17β-trihydroxyandrost-5-ene, 7-oxodehydroepiandrosterone, 16α-fluoroandrost-5-ene-17-one, 7α-hydroxy-16α-fluoroandrost-5-ene-17-one, 7β-hydroxy-16α-fluoroandrost-5-ene-17-one, 17α-hydroxy-16α-fluoroandrost-5-ene, 17β-hydroxy-16α-fluoroandrost-5-ene and the like.

Please replace paragraph 358 at page 118 with the following amended paragraph.

[00358] wherein (a) R_1 and R_2 are each independently selected from the group consisting of a hydrogen atom and $-O-C(O)-OR_{14}$, wherein (i) R_{14} is selected from

the group consisting of a hydrogen atom, optionally substituted alkyl, and a carbocyclic ring; and (ii) at least one of R_1 or R_2 is not hydrogen; (b) R_5, R_6, R_7, and R_8 are each independently selected from the group consisting of a hydrogen atom, optionally substituted alkyl, hydroxy, -O-C(O)-OR_{14}, and a protected hydroxy; or R_5 and R_6 taken together form an oxygen atom, which, together with the carbon atom to which R_5 and R_6 are joined is =O (a ketone); or R_7 and R_8 taken together form an oxygen atom, which, together with the carbon atom to which R_7 and R_8 are joined is =O; and (c) R_{12} and R_{13} are each independently selected from the group consisting of a hydrogen atom, alkyl, hydroxy, and a protected hydroxy. ~~Such compounds incl;ude ones wherein~~ Such compounds include ones wherein (1) the protected hydroxy is an ester, e.g., acetate or proprionate, (2) R_1 and R_2 are -H and -O-C(O)-OR_{14} and R_{14} optionally is methyl, ethyl, propyl, n-butyl, sec-butyl, t-butyl, n-octyl, n-dodecyl, 1-ethoxyethyl, 9-fluorenylmethyl or -C(O)CH_3, (3) R_5 and R_6 independently are -H, -OH, -O-C(O)-OCH_3, -O-C(O)-OC_2H_5, -O-C(O)-OC_3H_7, -O-C(O)-OC_4H_9, -O-C(O)-$OCH_2C_2H_3$, -O-C(O)-$OCH_2C_3H_5$ or -O-C(O)-O-$(CH_2)_2$-O-C_2H_5, (3) R_5 and R_6 are -H and -OH, e.g., R_5 and R_6 are -H and -OH or together are =O, (4) R_{12} and R_{13} are methyl, (4) R_7 and R_8 are each independently selected from the group consisting of a hydrogen atom, hydroxy, and trialkylsilyl, e.g., ~~R_7 and R_8 are are -H and -OH or together are =O~~ R_7 and R_8 are -H and -OH or together are =O. These compounds include 3β-carbomethoxyandrost-5-ene-7,17-dione, 3β-carboallyloxyandrost-5-ene-7,17-dione, 3β-carboethoxyandrost-5-ene-7,17-dione, 3β-carboisobutoxyandrost-5-ene-7,17-dione, 3β,17β-dicaromethoxyandrost-5-ene-7-one, 3β-carbooctyloxyandrost-5-ene-7,17-dione, 3β-carbo(9-fluorenyl)methoxyandrost-5-ene-7,17-dione, 3β-carbomethoxyandrost-5-ene-7,17β-diol, 3β-carboethoxyandrost-5-ene-7β,17β-diol, and 3β-carbooctyloxyandrost-5-ene-7β,17β-diol, or an pharmaceutically acceptable salt, ester, ether, amide, or prodrug thereof.

Please replace paragraph 359 at page 119 with the following amended paragraph.

[00359] The compounds of formulas V, VI, VII, VIII and IX can be incorporated into a ~~composition comprinsing the compound~~ composition comprising the compound and an excipient, e.g., an excipient disclosed herein. Such compositions are useful to treat subjects having or subject to developing the diseases, conditions or symptoms disclosed herein, e.g., obesity, diabetes, hyperlipidemia, infection, cancer, immune suppression conditions, inflammation or autoimmune conditions. The compounds can thus be used in a method of treatment comprising administering an amount effective of one of these compounds to a subject (e.g., a mammal or human) to treat the disease, condition or symptom or to ~~modulate the subjet's immune system~~ modulate the subject's immune system, e.g., to enhance a Th1 immune response or to modulate a subject's weight or to slow the progression of a disease or condition.

Please replace paragraph 392 at page 136 with the following amended paragraph.

[00392] Phosphothioesters, R^BO-P(SR^{PR})(O)-O- are generated by treatment of alcohols with the monothio analog of diethylchlorophosphate as described for phosphoesters yielding the phosphothioesters. Carbonates, R^BO-C(O)-O- are generated from the corresponding steroid alcohol using the chloroformate (R^B-C(O)-Cl), e.g., C_{1-20} alkyl, alkenyl or alkynyl chloroformates (e.g. $CH_3(CH_2)_{0-5}$-C(O)Cl). Carbamates, R^B-NH-C(O)-O- are made from steroid alcohols by treatment with isocyanates (R^BN=C=O) or NaOCN in the presence of trifluroroacetic acid. ~~Aminoacid esters, ZNX-CHY-C(O)-O- are~~ Amino acid esters, ZNX-CHY-C(O)-O- are generated by coupling the steroid alcohol with the acid chloride of the N-protected amino acid.

Please replace paragraph 433 at page 167 with the following amended paragraph.

[00433] The oily phase of the emulsions of this invention may be constituted from known excipients in a known manner. While the phase may comprise an emulsifier (otherwise known as an emulgent), it desirably comprises a mixture of at least one emulsifier with a fat or an oil or with both a fat and an oil. A hydrophilic emulsifier may be included together with a lipophilic emulsifier, which acts as a stabilizer. Some embodiments include both an oil and a fat. Together, the emulsifier(s) with or without stabilizer(s) make up the so-called emulsifying wax, and the wax together with the oil and fat make up the so-called ~~emulsifying ointment base which forms~~ emulsifying ointment base, which forms the oily dispersed phase of the cream formulations.

Please replace paragraph 435 at page 167 with the following amended paragraph.

[00435] The choice of suitable oils or fats for the formulation is based on achieving the desired cosmetic properties. ~~Creams are generally a non-greasy, non-staining~~ Creams are generally non-greasy, non-staining and washable products with suitable consistency to avoid leakage from tubes or other containers. Straight or branched chain, mono- or dibasic alkyl esters such as di-isoadipate, isocetyl stearate, propylene glycol diester of coconut fatty acids, isopropyl myristate, decyl oleate, isopropyl palmitate, butyl stearate, 2-ethylhexyl palmitate or a blend of branched chain esters known as Crodamol CAP may be used. These may be used alone or in combination depending on the properties required. Alternatively, high melting point lipids such as white soft paraffin and/or liquid paraffin or other mineral oils are used.

Please replace paragraph 1205 at page 365 with the following amended paragraph.

[001205] Treatment of HIV infected patients normalized their IL-10 producing $CD4^+$ T cells. In the same patients, 16α-bromoepiandrosterone was shown to enhance the proportion of $CD4^+$ ~~Tcells that express detectable~~ T cells that express detectable IFNγ . $CD4^+$ IL-10^- $IFN\gamma^+$ T cells mediate Th1 responses. These results show that the compound reduced the Th2 component of the immune system and enhanced the Th1 component.

Please replace paragraph 1218 at page 371 with the following amended paragraph.

[001218] In a separate clinical trial using 100 mg of BrEA delivered to patients once per day for ~~5 consecutive days by intramusular injection~~ 5 consecutive days by intramuscular injection, several patients were evaluated for changes in the ratio of $CD4^+$ memory T cell 1 cells (intracellular $IFN\gamma^+$ $CD45RA^-$ $CD62L^-$ $CD11a^{bright}$) or MT1 cells to memory T cell 2 cells (intracellular IL-4^+ $CD45RA^-$ $CD62L^+$ $CD11a^{dim}$) or MT2 cells. MT1 cells mediate or facilitate Th1 immune responses and MT2 cells mediate or facilitate Th2 immune responses. An increase in the MT1:MT2 ratio indicates an enhanced Th1 immune response or immune status. See, e.g., D.K. Mitra et al., *International Immunology* 1999 11:1801-1810. The tested patients (7/7) showed a transient increase in the MT1:MT2 ratio after a 5 day course of dosing with BrEA. The maximum observed increase was about 700% in one patient at 10 days after the last dose of BrEA was administered. The increase usually persisted for more than 10 days after the last dose of BrEA was administered. These results showed that BrEA was capable of enhancing the numbers of circulating immune cell subsets that mediate Th1 type responses.